EXHIBIT H

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

IN RE: VALSARTAN, LOSARTAN, AND IRBESARTAN PRODUCTS LIABILITY LITIGATION,	:	MDL NO. 2875
THIS DOCUMENT RELATES TO: Duffy, et al. v. Solco Healthcare U.S., L.L.C., et al., Case No. 1:18-cv-15076-RBK-JS	:	

VOLUME II
RESTRICTED CONFIDENTIAL

Veritext Virtual Zoom Videotaped deposition of MAHYAR ETMINAN, taken on Wednesday, August 25, 2021, held in Vancouver, City of British Columbia, Canada, commencing at 8:32 a.m., before Jamie I. Moskowitz, a Certified Court Reporter and Certified Livenote Reporter.

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MAHYAR ETMINAN

Examination

THE VIDEOGRAPHER: The time is now 8:32. This is a continuation of Mahyar Etminan's deposition. We are back on the record.

EXAMINATION BY MR. GALLAGHER:

Q Good morning, Dr. Etminan.

A Good morning.

Q At this time, I don't -- at this time I don't have further questions for you. Some of the other defense counsel do, so I'm going to turn it over to counsel for Mylan.

EXAMINATION BY MR. TRISCHLER:

Q Good morning, Doctor.

A Good morning.

Q I'll just start by introducing myself to you. My name's Clem Trischler. I represent the Mylan defendants in this litigation. I'll be asking you some questions following up on Mr. Gallagher.

If you can -- if you have any trouble hearing me, please let me know so I can rephrase or repeat the question. Okay?

A Okay.

Q Let me start by asking you this relatively simple and straightforward question, Doctor. Would you agree with me that NDMA and NDEA

are ubiquitous?

MR. NIGH: Form objection.

THE WITNESS: Yes, generally speaking.

BY MR. TRISCHLER:

Q Those compounds are found virtually everywhere, true?

MR. NIGH: Form objection.

THE WITNESS: Generally speaking, yes.

BY MR. TRISCHLER:

Q NDMA and NDEA are found in the air we breathe, in the water we drink and in the food we eat, correct?

A Yes.

Q In fact, I think you wrote in your report that NDMA and NDEA are found in pesticides, hair dye, air, water and food. That's what you wrote I think on Page 7 of your report, right?

A Yes.

Q So it's a known fact that each and every one of us are exposed to nitrosamines such as NDMA and NDEA on a daily basis, true?

A Yes.

Q And as part of your work in this case, have you attempted to quantify the baseline level of exposure to NDEA that the average American receives

on a daily basis?

A No, not personally.

Q Have you done any original research in your career that's been designed to determine or calculate the baseline daily exposure to NDEA?

A No.

Q Are you aware of the fact that there are studies that have been published in the peer-reviewed literature that suggest that dietary intake of NDEA and NDMA can be as high as 2,000 nanograms per day for the average American?

MR. NIGH: Form objection.

THE WITNESS: That -- I mean, that's possible. I don't remember of a specific paper, but that's possible.

BY MR. TRISCHLER:

Q Okay. And are you aware of the same studies suggesting that smokers have a daily intake of NDEA and NDMA that can be as high as 20,000 -- 25,000 nanograms per day?

A I'm not aware of studies, but it's possible that's the case.

MR. NIGH: Form objection to that question.

BY MR. TRISCHLER:

Q Assuming there are studies that suggest daily intake of nitrosamines for smokers can be as high as 20,000 to 25,000 nanograms per day, do you have any scientific basis to dispute that fact?

MR. NIGH: Form objection.

THE WITNESS: Well, I mean I have to -- I have to read the scientific paper and then see exactly how that number was derived. So I think you're asking me a very general question.

BY MR. TRISCHLER:

Q Well, I don't know whether it's general or specific. I'm just asking you a question, and the question is this: As you sit here today providing testimony under oath, are you aware of any evidence to suggest that daily intake of nitrosamines for smokers is something other than 20 to 25,000 nanograms per day on average?

MR. NIGH: Form objection.

THE WITNESS: I -- I don't -- I didn't look at nitrosamine exposure among smokers, so, again, this is -- this is not an area that I specifically looked at. I know generally speaking, smokers could have a higher

concentration of NDMA than nonsmokers.

BY MR. TRISCHLER:

Q And I think what you said as part of your research in this case and part of your work in this case, you did not do any analysis to determine baseline exposures for either NDEA or NDMA, right?

MR. NIGH: Form objection.

THE WITNESS: Yes.

BY MR. TRISCHLER:

Q Would you agree that if an individual consumes alcohol, his or her daily exposure to NDEA and NDMA would be expected to increase?

A Than a nonalcoholic, yes.

Q Well, not just a known alcoholic, but anyone that consumes alcoholic. I like a beer or two from time to time, and I don't think I'm an alcoholic. But when I consume alcohol, research suggests that my daily intake of nitrosamines is going to go up. Wouldn't you agree?

A It's -- yeah, it's going to go -- it's going to be higher than, you know, when you were not taking alcohol or compared to somebody who's not taking alcohol.

Q Sure, so -- so we can agree that there's a baseline of exogenous exposure to NDEA and

NDMA that all of us experience, right?

A Yes.

Q All of us have a lifetime of exposures to NDMA and NDEA, right?

A Yes.

Q Every plaintiff in this litigation has been exposed to NDMA and NDEA throughout their lifetimes just like you and I have, right?

A Yes.

Q In this case, though, you've done nothing to independently assess, evaluate or quantify what that baseline exposure is, right?

MR. NIGH: Form objection.

THE WITNESS: You're talking about me undertaking a study, looking at your question. That was not what I did or I was asked to do.

BY MR. TRISCHLER:

Q I understand. That's what I'm just trying to clarify. There were things were you asked to do and things you were not.

And one of the things you have not done is to quantify a baseline exposure for NDEA and NDMA for any plaintiff in this litigation or any average person in the community, right?

MR. NIGH: Form objection.

THE WITNESS: Yes.
BY MR. TRISCHLER:
Q Nothing in your report that's been filed with the court in this case quantifies baseline NDEA or NDMA exposures, agreed?
MR. NIGH: Object to form.
THE WITNESS: Yes.
BY MR. TRISCHLER:
Q And at the outset of yesterday when you were being asked questions by Mr. Gallagher, what I recall you stating is that what you were retained to do was to review the literature and provide an answer to the question of whether NDMA, regardless of route of administration, could plausibly cause cancer in humans. That was the question you were asked, and you -- and you undertook a literature review to try to answer that question, correct?
A Yes.
Q And while that was the question you were asked to evaluate, I think, as we have just established, there were other questions concerning NDMA and NDEA that you never examined, right?
A Well, what do you mean by "other questions"?

Q Well, for instance, we talked about the fact that you never researched the amounts of NDMA that the average American adult consumes on a daily basis, right?

A I do have in my report a citation of general range of exposure of NDMA in -- you know, in the American diet. And I agree with you that, you know, generally, they are all exposed to NDMA, you know, from the environment or from air or what have you.

Q Right. And I think you agreed with me that daily exposure is on the order of 2,000 nanograms per day. But my question was that was not the -- determining that average baseline exposure from dietary intake was not the question that you were asked to answer?

MR. NIGH: Hold on. Hold on. Object to form, mischaracterizes his testimony. Never was there an agreement that the average baseline is 2,000 nanograms of NDMA.

You can answer.

MR. TRISCHLER: I don't think speaking objections are permitted, Daniel, so please don't do it.

MR. NIGH: Well, you can't

mischaracterize testimony.

MR. TRISCHLER: Well, I think you can object to form, but let's not -- let's not start testifying, please.

MR. NIGH: Okay. Form objection.

THE WITNESS: Yes.

BY MR. TRISCHLER:

Q And you never researched the amount of NDEA that the average American consumes on a daily basis, right?

A Yes.

Q You have not reviewed the cases of any plaintiff in this litigation to calculate their cumulative -- cumulative lifetime exposure to NDMA or NDEA prior to the time they consumed any valsartan-containing medication, right?

A Correct.

Q Have you ever -- we have been talking about exogenous exposure, but have you ever independently researched endogenous formation of nitrosamines where the extent of endogenous formation that occurs prior to the time you were retained in this case?

A No.

Q And in connection with your work in

this case, have you ever done any research to try and answer the question of the extent of endogenous formation of nitrosamines that occurs in the human body?

A No. I mean, that -- that is not my field of expertise.

Q Understood.

Are you aware of any research suggesting that all of us endogenously form nitrosamines in our body at levels even higher than what we consume exogenously?

A I know that there is potential for endogenous formation of NDMA in -- in the human body.

Q Right. And in reading some of the studies that you cite in your report, and that you were kind enough to discuss with us yesterday, some of those studies suggest that the level of nitrosamines that form endogenously are far greater than what we consume on a daily basis, right?

MR. NIGH: Form objection.

THE WITNESS: Yes.

BY MR. TRISCHLER:

Q In fact, I think one of the papers that was cited in your report was a paper that was

published by a gentleman named Jakszyn as the lead author -- lead author, excuse me. Jakszyn is spelled J-a-k-s-z-y-n, I believe. Do you recall that paper?

A Yes.

Q I think it was entitled "Endogenous Versus Exogenous Exposure to Nitroso Compounds" and was marked as Exhibit 12, yesterday. Do you remember that?

A Right.

Q And according to that paper by Jakszyn, we're exposed to over 93,000 nanograms of nitrosamines every single day. Do you remember that?

MR. NIGH: Form objection.

THE WITNESS: I do remember that.

BY MR. NIGH:

Q And as part of your work in this case, you have not done any independent research studies or testing to -- to suggest or establish that the estimates of total nitrosamine exposure as predicted by Jakszyn were incorrect, fair to say?

A Yes.

Q And I trust you'd agree with me that if you want to evaluate the impact of nitrosamines

in valsartan-containing medications, what we need to consider is the extent to which individual consumption of NDMA and NDEA increase due to the presence of those compounds in the drugs, right?

MR. NIGH: Form objection.

THE WITNESS: I mean, if you want to do a perfect study, yes, that's -- that's what needs to be done.

BY MR. TRISCHLER:

Q And in assessing carcinogenicity of any compound, you agree that dose and duration of exposure are always important, right?

A Generally speaking, yes.

Q Right. Well, in fact, yesterday, we discussed the Pottegard and Gomm studies. Do you remember that?

A Yes.

Q And one of the things I remember from your testimony yesterday was that you were critical of those studies because the amount of NDMA exposure was not specified in the controls. Do you recall telling us that?

A Yes.

Q And you told us that, you know, for that -- in that study, you would have liked to have

seen the controls broken down by high exposure, medium exposure and low exposure. Do you remember telling us that?

A Yes.

Q And the inference from that is that you wanted them broken down that way because dose and duration are undoubtedly important and undoubtedly contribute to carcinogenicity, right?

A Yes.

MR. NIGH: Form objection.

BY MR. TRISCHLER:

Q And in this case, you've been very clear and very honest and open in telling us that you have not done any work to -- since you have not done any work to establish baseline exposures, right?

MR. NIGH: Form objection.

THE WITNESS: Yes, I think I have answered that already.

BY MR. TRISCHLER:

Q Right. And since you have not done any work to establish baselines, you can't tell us the extent to which any plaintiff's daily intake of NDMA or NDEA increased due to the use of valsartan-containing medications, right?

A Correct.
Q So if we -- I told you at the outset I introduced myself, my client is Mylan. If we use Mylan is an example. You reference my client I think only in one place in that -- in your --
THE COURT REPORTER: I'm sorry. You cut out.
BY MR. TRISCHLER:
Q I said you reference Mylan only in one place in your entire report. Would you agree?
A I believe it's the -- the part where I show the ranges of -- of NDMA in the product.
Q Agreed.
You -- you -- you provided us with a 40-page report, and the only place where you ever mention my client is in a footnote on Page 8, correct?
A Yes. I wasn't asked to write reports for different manufacturers.
Q I understand. But in that footnote, you suggest that NDEA concentrations in some of Mylan's products were found to range from .01 parts per million to 1.57 parts per million. Do you remember writing that?
A Yes.

Q And the -- as part of your work in this case, did you -- did you calculate the mean parts per million that was observed in Mylan's product?

A I remember I may have calculated either the mean or the -- or the higher range of the PPM.

Q Well, if you calculated a mean, what did you calculate?

A I don't remember off the top of my head. But I mean, if I can just do a quick calculation if you tell me what the -- if I can -- I'm just looking at my report.

Q Well, to calculate the mean, you'd need to know a lot more than just what the lower bound and what the upper bound of the range was, right?

A Yes.

Q Right. And the only information you have in your report is the low -- low range being .01 parts per million, and the high being 1.57 parts per million -- per million. So how would you calculate a mean? But you can't calculate a mean based on that. You'd need other data and other information.

A Yeah, I probably -- I probably just --
MR. NIGH: Hold on. Hold on. Let me object to the form first. Form objection.
You can answer, Doctor.
THE WITNESS: I probably only looked at the higher -- higher end of the 1.57.
BY MR. TRISCHLER:
Q So -- so your best recollection, sitting here today, is you never calculated a mean concentration of NDEA in the Mylan product, right?
A Right.
Q Well, I'll represent to you that the -- for purposes of my questions that the mean concentration for -- in Mylan's product is observed to be 0.047 parts per million, okay?
A Okay.
Q And if we assume the -- did you -- were you made aware of the fact that the largest concentration in which valsartan-containing medications or the largest dose in which valsartan-containing medications were made available in the United States was 320 milligrams per day?
A Yes.
Q And so if the mean is .047 parts per million, and we assume the largest dose of

320 milligrams, that results in a mean exposure of 150 nanograms, correct?

A Correct.

Q So going back to Jakszyn's data in Exhibit 12 that you -- in his paper that you included with your report, if his estimate of nitrosamine exposure of 93,000 nanograms per day is accurate, in 150 nanogram --

THE COURT REPORTER: I'm sorry. You broke up. You broke up.

MR. TRISCHLER: I'll start over.

BY MR. TRISCHLER:

Q If we assume the data from Jakszyn's paper is accurate, then adding a 150-nanogram exposure to a daily nitrosamine exposure of 93,000 nanograms is miniscule, correct?

MR. NIGH: Object to form. Object to form.

THE WITNESS: Well, again, we -- that's -- the Jakszyn study is one study. It has some limitations. Back to your -- back to your point, the 150, I believe the -- the Mylan nanogram per -- the mean Mylan nanogram per day of 150 is -- one has to look at this as a cumulative exposure. So patients would be

taking this over extended period of time. 150 is still higher than the -- the recommended or the allowable daily dose by the FDA.

And you are sort of assuming that only the patient who's taking the 150-nanogram Mylan dose has that endogenous exposure -- sort of exposure to endogenous nitrosamines as well. In other words, you know, in the population, as we spoke earlier, we are all exposed to nitrosamines. So population-wise, there is no reason to believe that the people who are not taking that extra dose of Mylan also do not have endogenous exposure to NDMA.

What I'm trying to say is that endogenous exposure in the population is probably very similar, at least in the American population, based on the diet. And if a patient is taking an extra dose of 150 nanograms per day of Mylan or any other exposures, an extra dose added to that baseline dose, which again is higher than the recommended daily dose by the FDA, cumulatively over a long period of time, it is possible that that dose could potentially increase the risk of cancer.

MR. TRISCHLER: Objection, move to strike as nonresponsive.

BY MR. TRISCHLER:

Q Let's see if we can try this again, Doctor.

A 150-nanogram exposure is miniscule compared to a 93,000-nanogram exposure, right?

MR. NIGH: Object to form.

THE WITNESS: Yes.

BY MR. TRISCHLER:

Q It's .01 percent of the total exposure, simple math, right?

MR. NIGH: Object to form.

THE WITNESS: Yes, but you are -- you are -- you're assuming that the -- that there is one patient taking -- exposed to endogenous X amount -- I don't know if the Jakszyn study is -- is the true endogenous value. But let's say there is an X amount of endogenous NDMA in one person. That person is being -- is adding to that, cumulatively, an extra dose. You're assuming that the other people who are not taking that extra dose do not have endogenous exposure, and only that patient has endogenous plus exogenous exposure.

What I'm trying to say that in a population, as we discussed, where diets are pretty stable, and this is in the U.S., for the most part, most people will have that baseline endogenous exposure. So the person who's taking the exogenous NDMA in valsartan, you'll have -- you'll have an added extra risk if you're taking it cumulatively every day.

So that -- that's what I was trying to explain to you.

BY MR. TRISCHLER:

Q I think I understand, Doctor. I'm not making the assumption that you believe I am. I agree with you 100 percent, that every one of us has exogenous and endogenous exposures to nitrosamines. And if Jakszyn is correct, that that exposure is on the order of 93,000 nanograms per day.

And so my -- so the issue in this case, then, is does an exposure of an extra 150-nanograms representing a .01 percent increase in that exposure level result in a substantial -- statistically significant increased risk of cancer. That's the question I want to answer.

And what I'm asking hearing from you is that's not a question -- I haven't asked the

question. That's not a question you ever answered in this case. You certainly don't answer it in your report, right?

MR. NIGH: Hold on. Object to the colloquy, argumentative.

You can answer.

THE WITNESS: So, again, as I mentioned yesterday, I'd love to answer that question. But the -- the type of question you're asking, data for that question, good data, is not available. What I was asked to do is to answer the question as a general causation question, does exposure to NDMA over time increase the risk of cancer. So that's what I -- that's what my systematic review addressed.

BY MR. TRISCHLER:

Q Understood.

A I did not -- I did not address mostly because I -- you know, I did search for the data. But that specific question that you're asking -- and it's quite more of an individual -- you know, individual causation question rather than a general causation question. So I did not answer that, the type of question you're asking.

Q Well, I agree with a lot of what you said. I disagree that it's not a general causation question.

But I think what we can really agree on is your statement that good data does not exist to answer the question of whether an incremental increase in nitrosamine exposures above the baseline that we all experience will lead to a statistically significant increased risk of cancer. It's not a question that you answered, and the data is not there to answer it. That's what you just told us under oath, right?

MR. NIGH: Object to form.

You can answer.

THE WITNESS: Again, I -- in my report, I -- I was asked to answer whether there is general causation with exposure to NDMA over time. That's what I answered in my report.

BY MR. TRISCHLER:

Q And you did not answer the question of whether an incremental increase over some period of -- over some period less than lifetime would lead to a statistically significant increased risk of cancer because the data is not there to answer that

question, agreed?

MR. NIGH: Object to the form.

You can answer.

THE WITNESS: I answered the question that NDMA exposure over time increases the risk of cancer. I did not answer the question of incremental increase, and I really don't understand what you mean by "statistically significant."

But I did not answer the question whether incremental increase of any specific doses of NDMA increased the risk of cancer. I answered a more general question of exposure, exposure over time versus cancer risk.

BY MR. TRISCHLER:

Q In your review of the scientific literature, did you find a single cohort or case control study that reported that a 1 to 2-percent increase in daily NDMA exposure would lead to a statistically significant increased risk of esophageal cancer?

MR. NIGH: Object to form.

THE WITNESS: Can you repeat the question, please?

BY MR. TRISCHLER:

Q In your review of the scientific literature, did you find a single cohort or case control study that reported that a 1 to 2-percent increase in daily NDMA exposure would lead to a statistically significant increased risk of esophageal cancer?

MR. NIGH: Object to form.

THE WITNESS: I don't know if the study looked at 1 to 2-percent increase, but there are -- the dietary studies that I included have looked at sort of a dose response exposure of NDMA per day, looking at high versus low doses with respect to cancer.

BY MR. TRISCHLER:

Q Can you cite me any study, as you sit here today, where the authors looked at incremental increases in nitrosamine exposure and concluded that a 1 to 2-percent increase in NDMA or NDEA intake would lead to an increased risk of cancer?

A Can you clarify --

MR. NIGH: Hold on. Hold on. Object to the form.

You can answer.

THE WITNESS: Can you clarify what you mean by "incremental increase"?

BY MR. TRISCHLER:

Q What I'm -- what we've been talking about, Doctor, that we all have a baseline of -- of exposure that we have been receiving on a daily basis. Let's assume that that baseline exposure is 2,000-nanograms. If we were exposed to 2,000-nanograms for the first 40 years of our life, and then in year 41, we begin to -- that exposure increases to 2,100 nanograms per day, what I want to know is: Are there any studies to suggest that an incremental increase in daily nitrosamine exposure is expected to lead to an increased risk of cancer?

MR. NIGH: Hold on. Hold on. Hold on. Hold on. Object to the form.

THE WITNESS: What I think you're -- you're referring to is whether -- whether there is a dose response increase with NDMA exposure and cancer so that the more NDMA you take over a period, your risk of cancer is higher.

So again, some of the dietary studies that I've discussed have looked at subjects who have taken the highest cumulative dose of NDMA in their diet and compared them to the -- to the lowest, considering that all of those -- all of that population is also exposed to some

level of endogenous NDMA through their diet.

They have looked at exogenous NDMA using dietary measures and looked at that dose response. So I think, again, your -- I think your question is whether there's a dose response relation. And I have shown in my report that some of these dietary studies have shown a dose response.

BY MR. TRISCHLER:

Q That's not -- that wasn't my question, but let me -- so let me try to ask it again.

Name me a study that's in your report or that you uncovered in your research that establishes that there is an increased risk of cancer if my nitrosamine intake is increased by 5 percent for a period of five years.

MR. NIGH: Sorry. Was that the end of the question?

MR. TRISCHLER: Yes.

MR. NIGH: Okay. Object to form.

THE WITNESS: Again, I think -- I think you're asking -- I think your question is asking the same concept of a dose response in a different fashion.

And so again, if -- the studies may

not have looked at nitrosamines in the way you're asking the question. But they have looked at those response. You're -- you're basically saying does somebody who has an increase in 1 to 2 percent over five years, does that person have a higher risk of cancer, and I think what -- and I think what you mean, and correct me if I'm wrong, is compared to somebody who doesn't have that 1 to 2 percent increase. That -- that is a dose response question, and I'm -- and that has been looked at in the dietary studies, not -- not exactly the way you have put it. But they have looked at cumulative dosing.

BY MR. TRISCHLER:

Q Well, I'm -- well, the way you phrased the question is the way I'm looking for you to answer it, Doctor.

And -- and so my question is, tell me the -- name me the dietary study where it says that a slight, short duration increase in nitrosamine exposure is gonna increase your risk for developing cancer. I can -- I read your papers, the papers you sent. I can't find it, so tell me where it is.

MR. NIGH: Object to form. This is

getting argumentative, lots of colloquy. It's inappropriate. It's not a question.

MR. TRISCHLER: It's a question. It might not be a good one, Dan, but it's a question.

MR. NIGH: But the -- "I've read your report. I can't find out where it is." You know, that's not a question. That's argumentative. It's inappropriate.

THE WITNESS: Again, the -- the -- the dose response analysis done in the dietary studies look at or present a dose response relation. They have not looked at it the way you have portrayed your question or the way you want the dose response to be looked at. But they have addressed -- I still think that your question -- your question is a dose response question. And they have addressed dose response in the way that all dietary studies address them, high dose versus low dose. What is the risk? Is there a difference in risk?

BY MR. TRISCHLER:

Q And what you're saying -- what you're suggesting with your answer is the same thing I think we already talked about, and that is that dose

and duration do matter, correct?

A Yes.

Q Right. And so what I'm trying to define is when does the dose and duration exposure to nitrosamines lead to an increased risk of cancer? Where do we draw the line? You have cited in your report -- you have got 71 references listed in this report, correct?

A Yes.

Q Tell me by number which one of those 71 references that I can go to that is going to suggest that if I increase my daily nitrosamine exposure by 5 percent or less for some period of time, that I'm -- I'm at an increased risk for cancer? Does that -- does that data exist anywhere?

MR. NIGH: Objection.

THE WITNESS: Again, the -- the way -- the question that you're asking me, that -- that type of analysis, I -- I did not find. But I did include, as you mentioned, dietary studies of the dose response analysis.

BY MR. TRISCHLER:

Q We talked about the fact that all of us are exposed to NDMA and NDEA on a regular basis, true?

A Correct.
Q But we can agree that while all of us are exposed to NDMA and NDEA every day, not all of us are going to develop cancer, correct?
A Yes.
Q So there's obviously a threshold dose or a threshold exposure at which NDMA and NDEA will not cause harm, agreed?
MR. NIGH: Object to form.
THE WITNESS: I -- I don't know. I don't know the answer to that question.
BY MR. TRISCHLER:
Q You have never calculated a threshold dose for NDEA, have you?
A Well, you're -- your question is not about the threshold dose on NDMA -- NDEA. I believe your question is whether there is a threshold dose in causing cancer, and so that requires another study. It's not as simple as just calculating threshold dose.
BY MR. TRISCHLER:
Q Well, I'm just asking you if you've ever done it.
A No, because that requires, again, a very large sophisticated study, and I -- I have not

done it. And I was not -- that's not what I was asked to do.

Q Are you familiar with the concept of permissible daily exposure?

A Yes.

Q Is it true that permissible daily exposure is defined as a dose that's unlikely to cause an adverse effect if the individual is exposed at or below that dose for a lifetime?

A I believe that's what it stands for.

Q Okay. Have you ever calculated a permissible daily exposure for any nitrosamine?

A No, because I relied on the epidemiologic studies that I looked at. I mean, the permissible daily exposure mostly comes from animal data.

Q I'm just asking if you have ever calculated a PDE for any nitrosamine?

A No. I appreciate that, but I just need to be able to explain myself. So, no, I have not.

Q Do you agree there is one though, right?

A There is one, for example, the FDA has one, yes.

Q Well, the FDA has an acceptable intake level that it's established for nitrosamine levels in drug products, but that's not a PDE, is it?

MR. NIGH: Object to form.

THE WITNESS: It may not be. I'll have to -- I'd have to check.

BY MR. TRISCHLER:

Q Well, just think about it. We've already -- we've already talked about and established that nitrosamines are ubiquitous and we're exposed to them from lots of sources, not just drugs, right?

A Yes.

Q Right. So there's a -- there's a permissible daily exposure for all nitrosamines including NDMA and NDEA. You've -- but you've not determined what they are, correct?

MR. NIGH: Object to form.

THE WITNESS: I don't know -- I mean, I could have during my research, but it doesn't ring a bell right now.

BY MR. TRISCHLER:

Q And you don't recall seeing any data suggesting a PDE for NDEA or NDMA, right?

A Correct.

Q Are you aware of any research that's been published in the peer-reviewed literature suggesting that a short-term increase in NDEA or NDMA exposure above the PDE will lead to an increased risk of cancer in humans?

MR. NIGH: Object to form.

THE WITNESS: No.

BY MR. TRISCHLER:

Q So if I could summarize what I understand your work in this case to be, Doctor, is that -- your focus was on addressing the general question of whether the literature supports a plausible causal connection between NDMA and cancer in humans, right?

MR. NIGH: Object to form.

THE WITNESS: Yes.

BY MR. TRISCHLER:

Q I didn't hear your answer because of the objection.

A Yes.

Q And your -- your research was not focused on dose or duration or on examining the impact of incremental increases in daily exposures, right?

MR. NIGH: Object to form.

THE WITNESS: Yes.

BY MR. TRISCHLER:

Q And now I want to ask you some questions specifically about NDEA. Before you were retained in this case, had you ever done any original clinical research on the carcinogenicity of NDEA?

A No.

Q For that matter, before you were retained by the plaintiffs' lawyers in this case, had you ever done any original clinical research on the carcinogenicity of NDMA?

A No.

Q Had you ever published any peer-reviewed studies assessing or evaluating the carcinogenicity of NDEA in humans?

A No.

Q Had you ever published any peer-reviewed studies assessing or evaluating the carcinogenicity of NDMA in humans?

A No.

Q Had you ever done any animal studies or participated in any animal studies looking at the carcinogenicity of any nitrosamine?

A No. I'm not a basic scientist, so no.

Q Okay. Had you ever participated in any epidemiological studies involving NDEA?
A No.
Q Had you ever participated in any animal study -- or excuse me. Have you ever participated in any epidemiological studies involving NDMA?
A No.
Q Prior to the time the plaintiffs' lawyers knocked on your door to ask you to work on this case, had you ever done any work in your professional career with nitrosamines?
A No.
Q So is it fair to say that in your career as a -- in the fields of pharmacology and epidemiology, that you never researched, studied or investigated the possible association of nitrosamines and cancers before you were retained in this case?
A I have done studies in the past on carcinogens and cancer, but not specifically on nitrosamines.
Q Right. And so since you had no specific background in studying, researching or investigating nitrosamines, the only basis for your

opinion as to whether NDMA or NDEA can cause cancer in humans is the literature that -- review that you did in connection with this case, right?

A Yes.

MR. NIGH: Object to form.

BY MR. TRISCHLER:

Q And in the -- with that literature review, I want to ask you specifically about NDEA.

Did you identify in your literature review any observational study in the literature that found a statistically significant association between NDEA and breast cancer?

A Specifically on breast cancer?

Q Yes, NDEA and breast cancer.

A No.

Q In your research for purposes of this case, did you -- can you identify any observational study that you found in the literature that reported a statistically significant association between NDEA and esophageal cancer?

A No.

Q In connection with your work in this case, can you identify for me any observational study in the literature that found a statistical -- statistically significant association between NDEA

and stomach cancer?

A No.

Q In connection with your work in this case, can you identify any observational study that you found in the literature that found a statistically significant association between NDEA and colorectal cancer?

A No.

Q In connection with your work in this case, can you identify any observational study in the literature that found a statistically significant association between NDEA and liver cancer?

A No.

Q In connection with your work in this case, can you identify any observational study in the literature that found a statistically significant association between NDEA and lung cancer?

A No.

Q In connection with your work in this case, can you identify any observational study that found a statistically significant association between NDEA and bladder cancer?

A No.

Q In connection with your work in this case, can you identify any observational study published in the literature that found a statistically significant association between NDEA and prostate cancer?

A No.

Q In connection with your work in this case, can you identify any observational study reported in the literature with a statistically significant association between NDEA and blood cancers?

A No.

Q In connection with your work in this case, can you identify any observational studies published in the literature that found a statistically significant association between NDEA and pancreatic cancer?

A I identified one study by Zheng that looked at NDEA and found an increase in risk.

Q And that -- that paper was -- the lead author was Zheng, Z-h-e-n-g, correct?

A That's right.

Q And that was published in 2018 in a publication called "Carcinogenesis"?

A Yes.

Q And would you agree with me that even while finding an association between pancreatic cancer and NDEA, the authors of the Zheng paper were careful to note that their observations were preliminary?

A That's what they may have stated in their paper, yes.

Q And isn't it true that the authors of that paper were careful to note that the findings and this reported association between NDEA and pancreatic cancer was merely preliminary?

A If that's what they said in their paper, then that's what they said, but -- I mean, that's what --

Q Well, you read -- you read it. Do you recall?

A I have read a lot of these papers. I can read it now. I don't recall that statement, but --

Q Isn't it true that the authors of the Zheng paper noted that their findings were preliminary and needed to be confirmed in a large prospective cohort study with consideration of sufficient time between diet assessment and disease diagnosis?

MR. NIGH: Object to form.

THE WITNESS: That is -- they are sort of portraying a perfect scenario. I'm not sure if -- and they call this preliminary. I'm not sure if there will ever be a large prospective study looking at this question again, but that's what they state.

BY MR. TRISCHLER:

Q Well, that was going to be my next question. Do you -- are you aware of the large prospective cohort study that Zheng and his colleagues recommended to be done, whether it was ever done?

MR. NIGH: Object to form.

THE WITNESS: I'm not aware.

BY MR. TRISCHLER:

Q We talked about my client, Mylan Pharmaceuticals, a bit and how you mentioned them in that footnote on Page 8.

Can we agree that nowhere in your 40-page report that you filed in this case did you ever conclude that an increase in NDEA intake in the amounts contained in Mylan's valsartan-containing medication to cause cancer in humans?

MR. NIGH: Can you repeat that? You

broke up. You broke up at the end.

MR. TRISCHLER: Sure.

MR. NIGH: Thank you.

BY MR. NIGH:

Q Can we agree that nowhere in your report you ever conclude that an increase in NDEA intake in the amounts contained in Mylan's valsartan-containing medications was sufficient to cause cancer in humans?

A Yes.

Q And you -- and in your work in this case, you have not found a single study in the peer-reviewed literature that would support a statistically significant increased risk of any cancer from a short-term duration nitrosamine intake increase of 150 nanograms per day, right?

A You mean a specific study that -- that looks at that specific dosage and cancer?

Q Yes.

A No.

Q The -- the -- are you familiar with the concept of latency periods in cancer?

A Yes.

Q Do you know what the average latency period is for esophageal cancer?

A Specifically for esophageal cancer, no.

Q Do you know the average latency period for stomach cancer?

A No.

MR. NIGH: Object to form.

BY MR. TRISCHLER:

Q Do you know the average latency period for colorectal cancer?

MR. NIGH: Object to form.

THE WITNESS: The latency period for cancer in general is usually around, give or take, ten years.

BY MR. TRISCHLER:

Q All right. I'm asking about specific cancer types, and if you don't know, you can simply tell me you don't know.

A Right. Again, I'm not an oncologist. So no, I -- I -- the answer to your question -- the last -- the answer to your last question on stomach latency is I don't know.

Q Okay. So and if I went through the nine cancer types that you mention in your report, would you know the average latency period for any of them?

MR. NIGH: Object to form.

THE WITNESS: Not specifically.

BY MR. TRISCHLER:

Q We talked a little bit about the Gomm -- or you talked a little bit about the Gomm and Pottegard studies yesterday. And we mentioned them again this morning. You're familiar with those papers, right?

A Yes.

Q And I think one of the things that you indicated to us was that you were critical of the observations by Gomm and Pottegard in their papers because the study durations too short; is that correct?

A Yes.

Q Basically what you -- what you said was that a study duration of -- with a study duration on the order of three, four and five years, it was simply too early to tell whether or not nitrosamines in valsartan-containing medications might have an increased risk of cancer, right? You need more time?

A Well, for a population-based study, it is short. But that doesn't mean that, you know, in some patients, a shorter onset of cancer cannot

occur. But when I'm looking at a -- obviously, this was a population study, the ones you're mentioning. And for a population study that median of three years is short.

Q I wasn't asking you about whether there's any particular individual that might have a shorter latency period than another. I was asking you about study design.

And what you told us yesterday was that a study period of four or five years, which I believe is the time frame in the Pottegard and Gomm studies is just too short, and it's too early to tell whether or not nitrosamines in valsartan-containing medications can cause an increased risk of cancer; you need a longer period of time to study that, right?

A Yes.

MR. NIGH: Object to form. Hold on. Hold on. Object to form. That was asked and answered.

BY MR. TRISCHLER:

Q That's what you told us yesterday, right?

A Yes.

Q Okay. And so in your opinion, how

long would you have to go out to find a credible study that evaluates NDMA and NDEA in valsartan-containing medications and whether those medications lead to an increased risk of cancer?

MR. NIGH: Form objection.

THE WITNESS: Certainly, more than, you know, five years.

BY MR. TRISCHLER:

Q Okay. What does that mean? Does it mean six years is enough, or do you have to go to like 10, 15?

A Well, again, you're asking me a technical question. So one has to sit down, and if you're looking at different types of cancer, you have to factor in the -- the different latencies of all the cancers that you want to study and then make sure that the follow-up period that you have in your study design meets those latency periods.

Q Okay. So are you familiar with a paper by Nadler, N-a-d-l-e-r, entitled, "Estimating Cancer Latency Times Using Weibull," W-e-i-b-u-l-l, "Model"?

A Doesn't ring a bell.

Q Are you familiar with the Weibull model?

A Yes.
Q What is it?
A A Weibull model is -- I believe it's a parametric statistical model.
Q For estimating latency periods?
A I -- again, that's a technical statistical question, but I believe it could be. It's a very general model that's used for different, sort of, outcomes and -- and one -- I mean, it could possibly be used for statistical modeling of latency as well. Because it looks at time, and latency is a time. You know, it's a function of time.
Q So I'll represent to you that in this -- in the Nadler paper using the Weibull model to estimate cancer latency times, the authors concluded that the average latency period for stomach cancer is 22 years. You don't have any information to dispute that, right?
MR. NIGH: Object to form.
THE WITNESS: I'm not going to agree right now on the latency period, which is quite a complex topic, based on just one paper.
BY MR. TRISCHLER:
Q I didn't ask you to agree to it. I asked you -- I made a representation to you of the

average latency period in the literature. And I asked if you have any basis to dispute it.

MR. NIGH: Object to form.

THE WITNESS: No, I have no basis to dispute it or agree to it.

BY MR. TRISCHLER:

Q Okay. And in -- in the same paper, the authors estimate the average latency period of lung cancer to be 13 years. Do you have any basis to dispute that?

MR. NIGH: Object to form.

THE WITNESS: Again, I can't agree or dispute.

BY MR. NIGH:

Q And so if we wanted to -- if we were an epidemiologist like yourself and we wanted to carry out, you know, a well-designed epidemiological study to evaluate whether nitrosamines in valsartan-containing medications led to an increased risk of stomach cancer, we'd need to carry that study out for 22 years, right?

MR. NIGH: Object to form.

BY MR. TRISCHLER:

Q If we assume that's the correct latency period?

MR. NIGH: Object to form.

THE WITNESS: It -- it will be -- it should be a study that has a very long follow up. Again, I don't want to be agreeing on numbers that -- that I haven't seen or from one paper. But generally speaking, it needs a long period of follow up.

BY MR. NIGH:

Q And so if we're going to be -- if we're going to approach the question of whether nitrosamines in valsartan-containing medications lead to an increased risk of cancer, we're going to make that determination based on the science, what you're telling us is we just don't know at this point because the -- we don't have enough time to answer the question, right?

MR. NIGH: Object to form.

THE WITNESS: To specifically design a study that looks at oral nitrosamine, it's going to be a complex study. But again, my report and my review was on a general causation of exposure of nitrosamine -- nitrosamines and cancer.

BY MR. TRISCHLER:

Q By the way, there are -- there are a

few other cancer types that are at issue in this litigation, breast cancer, kidney cancer, pharyngeal cancer and uterine cancer.

In your report, you did not observe any statistically significant increased risk between NDMA and NDEA exposure and breast cancer, do you?

A Again, I don't think a statistically significant increase is the right sort of portrayal. I did not include any studies, whether significant or not, because they did not meet -- those types studies did not meet my inclusion criteria, which --

Q So you don't -- I'm sorry. I didn't mean to interrupt you.

A Go ahead.

Q No. I thought you were finished.

A I -- sorry. I think I am finished.

Q I guess what I'm asking is you do not intend to offer an opinion that NDMA exposure or NDEA exposure will lead to an increased risk of breast cancer, do you?

A No, because it's a not in my report, and I did not cover -- cover this topic.

Q You do not intend to offer an opinion that exposure to NDMA or NDEA lead to an increased risk of kidney cancer, do you?

A No.
Q You do not intend to offer an opinion that exposure to NDMA or NDEA lead to an increased risk of pharyngeal cancer, do you?
A Well, I do have -- I do have oral cancers including larynx, I believe, in my report. So pharyngeal, specifically no, but I do talk about oral cancers, in general, including the larynx. And so, again, I do make an opinion on oral cancers in general. It does not specifically say pharyngeal.
Q Okay. But when you say "oral cancers," the only one I'm aware of that arguably constitute oral, at least as I understand the anatomy, is esophageal?
A No. Oral cancers can also include the mouth, the esophagus and also the pharynx and the larynx. So I do have a section in my report on pharynx, larynx and the esophagus, which I combine into head and neck cancers.
Q Okay. Do you intend to offer an opinion that exposure to NDMA or NDEA increase the risk of uterine cancer?
A No.
THE WITNESS: Can I interject?
MR. TRISCHLER: Yes.

THE WITNESS: Can we take a break now if you have more information to cover, but if you're reaching the end, maybe we can continue. Either option is okay.

MR. TRISCHLER: Well, I'm -- I'm reaching my end, but there will be another examiner, at least one other examiner that I'm aware of. So we can take a break.

THE WITNESS: No, I understand. I meant just your section.

MR. TRISCHLER: Yeah. You won't -- you won't -- we can take a break whenever you want. It won't mess me up, so you're in control of that. So you tell me.

THE WITNESS: I mean, if you have another 5, 10 minutes, we can go -- you know, we can continue. If it's longer, I'd like to take a break.

MR. TRISCHLER: No, I don't have any -- in fact, I think -- I think I'm probably finished, so I will pass the witness. If you want to take a break now then, or, you know, I'll leave that up to you and Daniel.

THE WITNESS: Sure. Can I take a break, everyone?

MR. NIGH: Yeah, let's take a ten-minute break.

THE VIDEOGRAPHER: The time is now 9:34. This ends Media Unit Number 1. We're going off the record.

(Whereupon, a short break was taken.)

THE VIDEOGRAPHER: The time is now 9:49 in this begins Media Unit Number 2 we're back on the record.

EXAMINATION BY MS. KAPKE:

Q Good morning, Dr. Etminan. My name's Kara Kapke, and I just have a few short questions.

You talked about how the -- one of the questions you were answering was whether NDMA or NDEA exposure over time increases the risk of cancer. Can you quantify the duration of time that you're talking about?

MR. NIGH: Form objection.

THE WITNESS: Different studies have different durations. So I can't really give you a specific answer.

I believe that -- in the range from maybe three or four years up to the study -- the occupational study, I believe had a 35 or 40-year follow up, so it is a big range.

BY MS. KAPKE:

Q So given that -- your answer, is it fair to say that a person would need to take NDMA or NDEA containing valsartan for at least three years before they had an increased risk of cancer?

MR. NIGH: Object to form.

THE WITNESS: No, I -- I wouldn't say that because, again, every -- it's a very -- latency to cancer is very individualized. And those are median follow-ups -- you -- which means that you have -- at each end -- you have a lower end and a higher end. So I can't -- I don't really want to make that specific sort of statement.

BY MS. KAPKE:

Q What are you willing to say, to a reasonable degree of scientific certainty, that is the -- minimum amount of time that a person would need to have taken valsartan that contained NDMA or NDEA before they are subject to an increased risk of cancer?

MR. NIGH: Form objection.

THE WITNESS: Again, given that I looked at general causation, I can say that exposure to NDMA and NDMA valsartan increases

the risk of cancer over time. I don't have any specific data to, sort of, give you a specific number right now.

BY MS. KAPKE:

Q You would agree with me that a person who took a single pill for -- you know, one -- one pill of valsartan that contained NDMA or NDEA would not have an increased risk of cancer, correct?

A One pill over what period?

Q One day.

A No.

Q You don't agree or you do agree with that?

A I agree with you that taking one pill of valsartan for one day does not increase the risk of cancer.

Q What about 30 days, so 30 days' worth of pills?

A 30 days, probably not as well.

Q I'm going to push it out. How about 90 days?

A Again, less likely.

Q Another way you -- you framed the question that you are evaluating was whether systemic exposure to NDMA could cause cancer.

Similar type of question, but what does "systemic" mean to you?

A Systemic means that NDMA that's available in -- in the body, and it's absorbed and available in the body to, you know, all the organs. All the organs are subject to some level of NDMA.

Q And have you ever put a quantification of the dose or the duration that it takes to reach that systemic exposure?

MR. NIGH: Form objection.

THE WITNESS: Can you repeat the question, please?

MS. KAPKE: Can the court reporter read it back?

(Whereupon, the testimony was read back as requested.)

THE WITNESS: No.

MS. KAPKE: Thank you very much, Dr. Etminan. I'll pass the witness.

THE WITNESS: Thank you.

EXAMINATION BY MR. FOWLER:

Q Good day, Dr. Etminan.

You may have seen me briefly yesterday. Let me just reintroduce myself. I'm Steve Fowler with the law firm Greenberg Traurig,

and we represent the Teva defendants. I've got some additional questions for you.

But let me just start very quickly. Am I correct that in -- in your research, nor in your report, did you attempt to determine whether the levels of NDMA and NDEA in the valsartan tablets at issue here, whether that level poses an increased risk of cancer?

MR. NIGH: Object to form.

THE WITNESS: Specifically looking at the levels, no. I made general sort of analogies based on the NDMA levels in the different manufacturers with respect to the -- the sort of a dose response relations that I found from the occupational and epi studies.

BY MR. FOWLER:

Q I see.

MR. FOWLER: By the way, Mr. Nigh, is there any reason that you're not on camera as a -- as a speaking role in this deposition?

MR. NIGH: We have had many of us that haven't been on camera on speaking objections, you know, the people that are handling the depositions. So I have seen it on multiple occasions from attorneys throughout this

litigation. So I'm not sure why at this point you're raising this issue, almost nine hours into the deposition.

MR. FOWLER: Well, you were initially yesterday, but if you're not comfortable, that's -- that's fine. I'll -- I'll leave it alone.

BY MR. FOWLER:

Q Dr. Etminan, let me shift gears here and go back to yesterday. I think your CV was marked as Exhibit 2. I'd like to -- to put your CV up.

MR. FOWLER: I don't know, Justin, if you can do that. I think it was Number 2.

BY MR. FOWLER:

Q Are you with me, sir?

A Yes.

Q Directing your attention to the top, you see the date of May 2021. Is that the date that you revised or updated your CV?

A Yes.

Q And when you did that, did you review your entire CV for accuracy and any changes that needed to be made?

A To the best of my ability, yes.

Q And you would -- you believe everything that you've stated on your CV is true and accurate to the best of your knowledge?

A Yes.

Q Do you recall what changes that you made or additions in May of 2021? Was it simply publications, or was it something else?

A No. It's usually just adding new publications.

Q Yes, sir.

Now, presently, according to your CV, you are an associate member in neurology, department of medicine; and associate member, department of anesthesiology, pharmacology and therapeutics.

What -- what responsibilities, if any, do you have in the department of neurology, for example?

A So as an associate member, my responsibilities are far fewer than my -- my own department, which is ophthalmology. For -- for neurology, I'm a reviewer for the journal -- movement disorder and epidemiology reviewer for the journal "Movement Disorder" where the editor in chief happens to be also in the department of neurology. So that's -- that's the connection.

Q And you are -- your title as associate professor in the department of ophthalmology is not because you had any education, training or experience in ophthalmology before changing to that department, correct?

A Correct. So the department of ophthalmology has clinical faculty who are ophthalmologists. Then they have -- and then they have research faculty, and I'm part of the research faculty.

Q Yes, sir.

And -- and prior to that, you were in the department of pediatrics; is that correct?

A Yes. Yes.

Q And you are no more a pediatrician than you are an ophthalmologist, right?

A Correct.

Q You simply acquire the title when you are transferred from one department to another?

A Well, the title doesn't -- I mean, title is assistant professor or associate professor, and then the department changes, right? So I'm not sure what you mean by "title."

Q Okay. Well, before, you were an associate professor in the department of pediatrics

at one point, the department of respiratory medicine at another point, correct?

A Correct.

Q But you have no medical training in either of those specialties, right?

A Correct.

Q And you call yourself -- or I've seen you call yourself an adjunct position in the department of pharmacology. Do you still contend that's your position?

MR. NIGH: Form objection.

You can answer.

THE WITNESS: In the department of pharmacology -- anesthesiology, pharmacology and therapeutics, yes.

BY MR. FOWLER:

Q Just to be clear, my question is, do you still believe that you have an adjunct position in the department of pharmacology at UBC?

A Yes.

MR. NIGH: Form objection.

BY MR. FOWLER:

Q And why do you call it adjunct? Are you teaching classes in the department of pharmacology?

A I -- I -- actually used to teach classes until last year. And I have some other collaborations with some of the faculty there, so that's why I do have the adjunct position.

Q I see.

Let's go to the second page of your CV, please. Sir, you indicate having received your PharmD at Idaho State University, and you note clinical pharmacology next to it. Are you with me?

A Yes.

Q The PharmD program at Iowa [sic] State does not have a separate program or separate degree or track for clinical pharmacology, does it?

A Idaho State. No. I put clinical pharmacology because many don't really understand or know who are non-pharmacists what a PharmD entails. And so I put clinical pharmacology just to explain what the degree entails, not specifically on a specific clinical pharmacology program.

Q Right. So you're not holding yourself out as having received some special PharmD degree in clinical pharmacology. Those are just the words you self-selected to describe your degree, correct?

A Correct.

Q And likewise -- and also, sir, you

testified yesterday you started your PharmD degree at University of British Columbia, but then you testified that you left. You, kind of, mentioned a couple of reasons.

One of them, you indicated the program was shorter at Iowa State. You would get your degree -- at Idaho State. You would get your degree faster. Is that your testimony, sir?

A I don't recall exactly what I said yesterday, but I could clarify.

I believe I did say that the UBC pharmacy program was clinically oriented, and I wanted to pursue a research career. So I -- I didn't see a fit there. And possibly, it was -- it was a more, perhaps, busier, if you will, stringent program that I didn't think I would really benefit from. So that's why I completed my degree at Idaho.

Q And there's not another reason that you left UBC that's a nonacademic reason, sir?

A No.

Q And the Idaho State University degree is four years just as UBC, correct?

A It was a two-year -- two years post baccalaureate program.

Q I see.

Your master's, your MSC from University of Toronto, is it your contention that that was specifically in clinical epidemiology, or is that, again, your choice of words to describe it?

A It was in clinical epidemiology.

Q And that was the degree that was specifically conferred, sir?

A I believe so.

Q And is it your contention that you were in a postdoc fellowship specifically in pharmacoepidemiology at McGill as opposed to a postdoc fellow in pharmacy?

A No, it was specifically pharmacoepidemiology.

MR. FOWLER: You can take that down. Thank you.

BY MR. FOWLER:

Q Now, sir, when you conduct research projects when you seek to determine what subject you're going to investigate, you testified yesterday that you look to various areas defined -- "emerging issues," perhaps, that you wanted to investigate. Is that a fair characterization?

A Yes.

Q And you mentioned media as one source

as well as health regulatory agencies, right?

A Correct.

Q But you also purposefully do studies with an eye towards assisting in litigation, correct, sir?

A I -- I wouldn't say that -- that's something I do systematically, no.

Q Doctor, have -- have you testified that you have contacted lawyers in the course of starting a study because you believe that that was going to be useful to them in litigation?

MR. NIGH: Form objection.

THE WITNESS: There could have been one occasion where I was in the process of doing the same sort of study, and a lawyer may have approached me at, sort of, the same timing.

BY MR. FOWLER:

Q I see. And you have done that with the Mirena IUD litigation?

A Yes.

Q Bear with me, sir. I apologize.

And you have never contacted a drug company to offer any benefit of your study or your expertise, only plaintiff lawyers, correct?

MR. NIGH: Object to form.

THE WITNESS: Again, I -- I am not -- you're sort of portraying it as I'm contacting lawyers. The Mirena situation, as I mentioned to you, was a situation where I was starting to question because it was in the media, and I was approached, sort of, in the same time by -- by -- by a lawyer.

With respect to approaching manufacturers, no, I have not. But I know that my research has been used by them in their defense.

BY MR. FOWLER:

Q You have never been retained by a pharmaceutical company as an expert in any matter; isn't that correct?

A No. I -- probably because a lot of my studies where I show an increase in risk with a drug, you know, they -- they don't, probably, want to retain me. So that's why -- that's one of the reasons I believe I have not been retained.

Q And they have never -- well, strike that.

You've only been retained by counsel for plaintiff in litigations involving

pharmaceuticals; isn't that correct?

A Yes.

Q And you withdrew from a case where you were retained by plaintiffs' counsel, you said yesterday it was because of the science. But isn't the reason that you withdrew from Copley v. Bayer was because you weren't happy with your -- with the lawyer you were working with?

A That could have been one of the reasons as well.

Q Sir, do you recall testifying that as a consultant for plaintiffs in the Risperdal litigation that you were paid approximately $200,000?

A I don't -- that number, I don't recall that number. I'm not sure if that's an accurate number.

Q Have you testified that your annual lawyer consulting income is 20 to $30,000 a year, at least in 2017, sir?

A That -- I may have mentioned that as an approximation, but -- but I don't really know what that $200,000 figure is coming from.

Q Have -- has your consulting with plaintiff lawyers increased, decreased or stayed the

same since 2017, sir?

A Since 2017, I would say it -- I would say it may have increased.

Q And other than the matter for ranitidine that you were instructed not to discuss further yesterday, do you have other pending litigation matters that you are involved in? I'm not asking what at the moment, sir.

A You just want to know if I am involved in other litigation?

Q Yes, sir.

A Yes.

Q Okay. About how many? If this is one and ranitidine is two, how many others?

A I just have to think about it. I have to count them. When you say "litigation," do you mean just the -- sort of the -- the topic area or how many different perhaps groups or lawyers?

Q What would be the best way for you to describe how many other topics that you are working with lawyers on presently other than the two I have mentioned?

A I would say two other topics.

Q Okay. Do you have any other depositions scheduled, sir?

A No.
Q Prior to your deposition, counsel for the plaintiffs provided some documents to the defendants, and what I'd like to do is just mark that entire set of documents as an exhibit. Then there may be some that I pull out.
MR. FOWLER: Can we do that, Steve? Can we mark that entire production as -- as the next exhibit?
MR. HARKINS: That will be marked as Exhibit 28. It may take a moment to upload.
MR. FOWLER: Thank you.
THE WITNESS: Can I take a two-minute break if you don't mind?
MR. FOWLER: Absolutely, Doctor. You're in charge. Off the record.
THE VIDEOGRAPHER: The time is now 10:12. We're going off the record.
(Whereupon, a short break was taken.)
(Whereupon, Exhibit 28 was marked for Identification.)
THE VIDEOGRAPHER: The time is now 10:15. We're back on the record.
BY MR. FOWLER:
Q Doctor, I would submit that Exhibit 28

is a composite exhibit of documents that were provided by counsel for plaintiffs to the defense counsel prior to your dep.

Did you have any role in deciding, for example, which articles would be included in that set of documents?

MR. NIGH: Form objection.

THE WITNESS: Yes. So I included documents that weighted heavily in my report and the opinion presented in my report. So all the major studies that I relied on, my search strategy are all included.

BY MR. FOWLER:

Q And where did you get copies of those articles?

A I ascertained the articles through the UBC library, electronic library.

Q Yes, sir.

MR. FOWLER: Let's mark as Exhibit 29 the search criteria documents, if I can refer to those as such. Are you with me, Doctor? Do you know what I mean?

(Whereupon, Exhibit 29 was marked for Identification.)

THE WITNESS: Which exhibit is this?

MR. FOWLER: It will be 29. Bear with me. It's going to come up.

BY MR. FOWLER:

Q And as it's posting, Doctor, you would agree that you attempted to set forth in the documents we're going to look at, your quote/unquote search methodology for selecting documents to review for your report; is that a fair statement?

A Yes.

Q And other than the searches that we're going to look at here that are described for the various cancers, was there any other medical database that you reviewed or other research you did to select articles other than what was the product of this search criteria that we're going to look at here on Exhibit 29?

A So as I mention in my report, I also looked at -- I used Google Scholar using the same terminologies. And I found pertinent articles through reviewing the articles that I -- I had found in case they were not listed in my search.

MR. FOWLER: How are we doing on Exhibit 29?

THE WITNESS: I'm looking at it.

THE VIDEOGRAPHER: Yes, it's up. I

was just waiting for the doctor.

MR. FOWLER: Okay. Because I'm not seeing it. There we go.

BY MR. FOWLER:

Q Okay, sir. So let's first orient ourselves to this. Can we scroll to the second page? Do you see we have bladder cancer there, Doctor, in the next page?

A Yes.

Q And brain -- brain tumors.

You're not offering any opinion that NDMA at the levels contained in the valsartan pills caused brain tumors, are you?

A No, but I --

Q Let's go to the top the first page.

MR. NIGH: Hold on. Hold on. You interrupted his answer. You gotta let him finish.

MR. FOWLER: I'm sorry. He answered no.

MR. NIGH: No. No. No. He was not finished. He said, "No, but," and you just spoke up. You gotta let him finish.

BY MR. FOWLER:

Q I'm sorry, Doctor. Go ahead.

A Because I did a systematic review of the literature of NDMA with all types of cancer, I included all types of cancer in my original search. And then I -- and after I looked at the evidence and synthesized the evidence, then I chose, depending on the amount of data that I had, which cancers to include and which not to include.

So, again, to be thorough and systematic, I did include all types of cancers in my search. But depending on the type of data and whether the data met my inclusion criteria, then I went ahead and mentioned in the report or included data for that in the report.

Q I see.

MR. FOWLER: Let's go to Page 1 of Exhibit 19 -- I mean, Exhibit 29. Now -- thank you.

BY MR. FOWLER:

Q What we're looking at here, Doctor, and -- is this a document that you created, or is it -- is it a printout, if you will, from your search engine?

A It's a printout. It's an electronic output of the search that I did.

Q Okay. Thank you. And what does the

EXP mean?

A It means expanded.

Q And what -- what you do you understand expanded to mean?

A So that -- that -- basically, it looks at all terminologies that would be related to nitrites, all different chemical -- chemicals that may be tagged in the database as nitrites just to be -- to make sure that nothing is missed.

Q So do I understand, in Line 1, that your search would have included not only NDMA, but any nitrosamines?

A Yes, because NDMA by itself does not have --

THE COURT REPORTER: I'm sorry. Does not have a what?

THE WITNESS: They don't have a MeSH M-e-S-H, which stands for medical subject heading. I believe it's -- I believe it stands for medical subject heading.

Anyway, it's the -- it's the key medical terminologies that are tagged by the National Library of Medicine, PubMed. So NDMA does not have a specific tag, but it's tagged under "nitrosamines."

So, again, to be ensuring that I'm not missing anything, I started the search with nitrosamine, which is the bigger umbrella term. But then I restricted at the end my inclusion for studies that -- specifically with NDMA.

MR. FOWLER: Let's go to the next page.

BY MR. FOWLER:

Q So for bladder cancer, sir, as I read this, again, your 120 articles that come out of -- at Line 8, include anything to do with nitrosamines or nitrites or NDMA, right?

A Right. So then what I -- what I did was, go through the 120 articles, which would have been animal studies where they could have looked at NDMA, NDEA or other nitrosamines. But then I only selected those that met my inclusion criteria, which is specifically looking at nitrosamines, NDMA or NDEA.

MR. FOWLER: Next page, please.

BY MR. FOWLER:

Q So there are 120 articles you said you reviewed there, correct?

MR. NIGH: Form objection.

BY MR. FOWLER:

Q Correct, Doctor?

A Yes.

Q And same question here for the brain tumors, it's your contention that you reviewed 64 articles looking for NDMA or NDEA?

A Yes.

MR. FOWLER: Next -- next page.

BY MR. FOWLER:

Q And for breast cancer, is it your contention you reviewed the 115 articles that are on line 16 looking for NDMA and NDEA?

A Yes.

MR. FOWLER: Next page.

BY MR. FOWLER:

Q You contend there are 130 articles that you looked through here?

A Yes.

Q And you did this all -- let me ask it differently.

Did you use any kind of electronic search method as you're reviewing these several hundred articles, sir?

A No. I just went through them, read the title of the article, read the abstract and then

decided whether they would meet my inclusion criteria or not.

Q And with regard to your inclusion criteria, you mentioned yesterday that it was important to you that the -- if NDMA is mentioned, that it be quantified when it's mentioned. Is that an accurate statement of your testimony yesterday, sir?

A Yes.

Q It was important to you that there be a measure of NDMA, not just a broad reference to NDMA. Does that make sense to you?

A Yes.

Q Okay.

MR. FOWLER: Next page, please.

BY MR. FOWLER:

Q And Doctor, of course, you -- you billed for all your time reviewing these 6, 7, 800 articles, didn't you?

A It was part of my work that I bill for it, yes.

Q And you would have reviewed all of these before you put pen to paper for your report?

A I'm not sure. I mean, either before or maybe during the time I was writing, perhaps, say

the introduction of the report, but definitely prior to the time where I sort of formed -- you know, formulated my opinion on the different types of cancer.

Q And is it your testimony that you can't go to PubMed and put in "NDMA" and "cancer," that it's not going to give you any results? Is that what you're saying?

MR. NIGH: Form objection.

THE WITNESS: It will give the results, but -- but it may not give you accurate results. There could be studies that may not be included in that search strategy.

BY MR. FOWLER:

Q So you didn't do it?

MR. NIGH: Object to form.

THE WITNESS: No, because, again, I wanted to be more thorough and do a -- do a more systematic approach.

BY MR. FOWLER:

Q Okay. Okay. And when -- let's say here in esophageal cancer, in those 19 articles, if you came across one or two that looked good to you, would you stop there, or would you look through all 19?

A I'm not sure what you mean by "looked good." So I went through the 19, and all from -- from the denominator of the 19 articles, whichever met my inclusion criteria was reviewed.

Q Okay. And did you electronically slide those over to some file on your computer? Did you print them? What did you do with it once you identified an article?

A I -- I tried to look at the -- or find the PDF versions so I could read them, and then I would -- I saved them in files under different, you know, sort of cancers.

Q I see.

And what if it -- let me start that again.

Did you have to purchase any of the articles that came up?

A No.

Q If -- if, for example, your search in PubMed came up with an article that required purchase, did you just move on to the next article?

A No. I would not leave important data because it could not be purchased. I would try to get it through --

THE COURT REPORTER: Through what?

Through what? You would get it -- you would get it through what?

THE WITNESS: Interlibrary loan service.

BY MR. FOWLER:

Q And, Doctor, for each article that you contend met your inclusion criteria -- let's stick with esophageal cancer here -- did you cite all of those articles in your report?

A No, I only cited, again, the articles that met my inclusion criteria.

Q Well, that was my question, sir.

Let's say esophageal cancer, there were 9 out of the 19 that met your inclusion criteria. Would you have cited all 9, or did you have another cut as to what you were going to cite?

A No. If -- if they met the inclusion criteria, I mentioned them.

THE COURT REPORTER: Counsel, can we go off the record for one second?

MR. FOWLER: Certainly.

THE VIDEOGRAPHER: The time is now 10:29. We're going off the record.

(Whereupon, a short break was taken.)

THE VIDEOGRAPHER: The time is now

10:29. We're back on the record.
BY MR. FOWLER:
Q Doctor, do you recall yesterday when we were talking about your report and that Table 1 on Page 15, you testified that you determined the -- the level of an unmeasured confounder that would be necessary to change the relative risk reported for an individual cancer? Did I get that right?
A Yes.
Q And you used this E-value methodology that you referred to in your report, right?
A Yes.
Q And with regard to the E-value methodology, do I recall your testimony correctly that the E-valued methodology can't be applied if there's more than one unmeasured confounder?
A Yes.
Q And so if -- in Table 1, if there was more than one unmeasured confounder amongst, let's say, the Hidajat study that you pulled from, this table would be moot, correct?
MR. NIGH: Form objection.
THE WITNESS: If there was a true unmeasured confounder, and we talked a lot about this topic yesterday, then this -- again,

this method is only designed to look at one.
BY MR. FOWLER:
Q Yes, sir. And you would consider that a limitation of the E-value methodology, sir?
A Yes.
Q Okay. Are you aware of other limitations to using an E-value methodology?
A The E-value methodology, like any epidemiologic tool, has -- or carries a number of assumptions. So, yes, it does have some assumptions built into it. But I think that overall, it is a widely accepted methodology.
Q Okay. Thank you. I think that was an answer to a different question. Let me ask my question. Listen carefully, please.
Are you aware of any limitations to using the E-value methodology, yes or no, sir?
MR. NIGH: Form objection.
THE WITNESS: What do you mean by --
MR. NIGH: Hold on. Hold on. Form objection and argumentative.
You can answer.
THE WITNESS: Can you -- can you clarify what you mean by "limitations"? One limitation we just agreed on is that it only

looks at -- it can only quantify one unmeasured confounder.

BY MR. FOWLER:

Q Okay.

A What -- what -- what other limitations? Can you -- if you could just elaborate on that wording.

Q Well, that's exactly what I'm asking you, sir.

You expressed limitations about all sorts of studies yesterday, and I'm asking about this methodology. You know what the term "limitations" means, right, sir?

A Yes.

Q Okay. What other limitations -- and if you don't know, that's fine. Are there other limitations of the E-value methodology?

MR. NIGH: Form objection.

THE WITNESS: Again, one limitation is what we spoke about. The other limitation is that the unmeasured confounder has to satisfy a couple of other sort of criteria for the -- for the E-value to work, but that's just like any statistical model that is -- are based on assumptions.

BY MR. FOWLER:

Q Are you aware of any articles critical of applying the E-value methodology?

A There have been articles talking about its limitations, yes.

Q And did you review those prior to applying the E-value methodology here to make sure it was a good fit?

A No. Because again, it is an accepted methodology used despite -- I mean, limitation is a -- is a very complex term. There could be limitations to a methodology, but it's still -- the limitations do not outweigh its strengths. And then there are limitations where you should not really use a specific approach.

In this case, there are limitations, but I think that if -- the strengths of the methodology outweighs its limitations. And that's why it's widely used as one way to assimilate what would happen to the effect size in the absence of an unmeasured confounder.

Q And, Doctor, for each of the cancers in your Table 1 where you drew the -- the -- let me start that again.

For each of the cancers listed in

Table 1 where you have attempted to apply the E-value methodology, if there is an unmeasured confounder for any one or all of those cancers, your conclusions from Table 1 would be null and void; they would be moot, correct?

A No. That's not what Table 1 means.

Q Table 1, the magnitude of hazard ratio on your right-hand column is derived using the E-value methodology, correct?

A It's the magnitude of the hazard ratio of the unmeasured confounder necessary to make the hazard ratio on the left null, so for the first cancer, for it to go from 1.72 to 1.0.

Q Yes, sir. Thank you.

And if that stomach cancer there is a second unmeasured confounder that you would not be able to calculate -- strike that -- you would not be able to apply the E-value methodology. I thought we established that; am I right?

A Correct.

MR. NIGH: Form objection.

BY MR. FOWLER:

Q Okay.

THE COURT REPORTER: Counsel, I'm sorry. Can we just go off the record for one

more second?

MR. FOWLER: Sure.

THE VIDEOGRAPHER: The time is now 10:36. This ends Media Unit Number 2. We're going off the record.

(Whereupon, a short break was taken.)

THE VIDEOGRAPHER: The time is now 10:37. This begins Media Unit Number 3. We're back on the record.

BY MR. FOWLER:

Q Doctor, from the Hidajat study on the rubber workers, you agree that they were exposed to multiple carcinogens, correct?

MR. NIGH: Object to form. I think that's the 21st time that question has been asked.

MR. FOWLER: Well, it was just a foundation because I was shifting gears, sir.

BY MR. FOWLER:

Q Right, Doctor?

A Correct.

Q And you have not and cannot draw any conclusion that any of the workers who expired in that study died from NDMA cancer, NDMA-induced cancer, correct?

A Can you repeat the question, please?
Q You cannot tell -- and the authors of this study made no -- reached no conclusion that any of the workers who died during this study period died as a result of NDMA-induced cancer; isn't that correct?
A Well, the study actually showed elevated risks of death secondary to high NDMA use versus low NDMA use in the different types of cancer. That's what the study actually set out to do. I'm -- I'm missing your question. I'm sorry.
Q Okay. I'll just withdraw that and move on.

Sir, you testified yesterday that the mechanism of cancer with exogenous exposure may take longer follow up than for endogenous exposure. Do you recall that testimony?
A I do. If I could clarify.
Q I really -- I only had that one question, if you recall testifying.

And so my follow-up to that is, you further testified that you believe it takes longer because you have to take it longer. It has to be digested and absorbed. Do you recall saying that?
A Well, now that I think about it, I'd

like to clarify that endogenous -- endogenous NDMA or nitrosamines or NDMA, nitroso compounds in general, I mean, they are already in the body. But they have -- they have been -- they got into the body from the outside, from the environment, from our food.

So now that I think about it again, I believe both exogenous and endogenous may take time for -- you know, for their effect to take place with respect to cancer.

I think the reason I said what I said yesterday is it was in reference to the Jakszyn study because the Jakszyn study had data on endogenous nitrosamines, which means that they had already been there and measured in that population.

But they had to get there somehow in the body, and that's probably through, again, outside. So a lot of endogenous NDMA could initially be exogenous, and it's just a matter of when you're measuring, you know. When you're measuring NDMA, you're measuring somebody's blood, and there is NDMA in there, that would be endogenous. But they have to be taking it from the outside to -- for that NDMA to get into the body.

So I'm not sure if I answered your

question, but I just wanted to clarify on endogenous versus exogenous.

Q Thank you, Doctor.

And if I understand what you just said, you believe that -- that endogenous levels of NDMA at some point started from the outside? Is that what you're saying?

A I think so, because as we've discussed, they -- NDMA is in the environment, and it gets into our body eventually. So I'm not aware of any mechanisms that the body itself creates endogenous NDMA. It has to be brought into our body from -- exogenously, if you will.

Q You're not aware because you're not a toxicologist, correct?

A No.

Q This is completely outside your field of education, training or experience to be commenting on endogenous NDMA, correct, sir?

MR. NIGH: Object to form. He's been asked numerous questions about this.

You can -- you can answer.

THE WITNESS: I -- I -- again, I was asked about endogenous NDMA with respect -- in an epidemiological studies context. I did not

opine, nor did I -- was I asked, I believe, to opine about, you know, toxicologic -- toxicological aspects of endogenous NDMA. It was just in the context of that one study -- study that we discussed yesterday.

BY MR. FOWLER:

Q Okay. Thank you.

And, Doctor, am I correct that you are unaware of the mechanism by which NDMA can be a carcinogenic substance in animals, for example?

A Well, from the literature that I have read and I have included in my report, it's through genotoxic mechanisms and potentially through other mechanisms that would qualify as a promoter for cancer.

Q You are not -- you have never published on quote/unquote cancer promoters, have you, sir?

THE COURT REPORTER: Cancer what?

MR. FOWLER: Promoters.

BY MR. FOWLER:

Q Right?

A No, that's not my field. What I was -- what I was trying to say is that for the biological plausibility section of my report and my

readings, I have reviewed some basic science cancer studies to form my opinion about the mechanism of NDMA cancer.

Q And you do not have an opinion whether any of the NDMA or NDEA contained in valsartan products ever leaves the liver, correct?

MR. NIGH: Form objection.

THE WITNESS: I cannot -- I don't have an opinion on that.

BY MR. FOWLER:

Q And if it doesn't leave -- did you consider what body systems -- what tissue systems NDMA that is ingested in -- with an oral -- orally ingested in tablet form, did you make any attempt to consider what parts of the body that oral ingestion may reach at the level of exposure in the pill?

A I believe that's a --

MR. NIGH: Hold on. Hold on. Hold on. Hold on.

Are you done with the question?

MR. FOWLER: I am.

MR. NIGH: Okay. Form objection.

You can answer, Doctor.

THE WITNESS: I believe that's a more of a basic pharmacology toxicology question

you're asking me. That's not my field, and I did not look at that.

BY MR. FOWLER:

Q Does -- does exposure to a chemical that -- that is being studied, does exposure affect the biologic plausibility in any attempt to evaluate the biologic plausibility, sir?

MR. NIGH: Form objection.

THE WITNESS: Can you clarify?

BY MR. FOWLER:

Q Sure. Does the method of exposure affect the analysis of biologic plausibility when assessing if exposure can lead to cancer?

MR. NIGH: Form objection.

THE WITNESS: Yes, it could.

BY MR. FOWLER:

Q Doctor, the Hidajat study used a sub-distribution hazard analysis; is that your recollection?

A That's right.

Q And given that it was over the course of 49 years of observation, the 94.1 percent of the study had died, would you agree it's very difficult to determine cause of death?

A I disagree because this was one of the

few papers that actually -- what the sub-distribution hazard that you explained does is actually controlled -- it calculates the hazard of death. It controls the hazard of death due to cancer from death due to other causes. And this was rightfully done -- because of the very long follow up, it's likely that these men could die of other causes.

And if you don't take that into account, you may actually see a protective effect from any exposure, because people are not surviving long enough to get cancer. And so the sub-distribution hazard -- it's called sub-distribution hazard because it comes from a sort of a -- I don't want to say different, but a more sophisticated model that takes into account death due to other causes.

Q Do you know how to calculate a sub-distribution hazard ratio?

A I'm familiar with the methodology, and the modeling that -- they have the equation in their paper actually.

Q But you've never done it?

A I don't think I have done it --

MR. NIGH: Hold on. Hold on.

Form objection. I can't tell, "you've never done it," calculated whenever or from that study. Form objection.

MR. FOWLER: Thank you for clarifying, Counsel.

BY MR. FOWLER:

Q Dr. Etminan, you have never, yourself, made any such calculation of a sub-distribution hazard ratio at any time, correct?

A No, because I haven't done studies that have such a long follow up. So I have not done it myself, but I'm familiar with the methodology.

Q Okay. Sir, yesterday, we talked -- or you talked a good bit about the relative risk calculations and your opinions with regard to when there is a wide confidence interval. Do you recall those -- that testimony?

A Yes.

Q And you -- you said that it was a wide confidence interval because of a small sample size? Is that -- is that what you believe?

A Well, sometimes it is a sample size, but it's actually more a function of number of cases or cancer cases, which sometimes can be a function of sample size, sometimes not. So if I want to be

more precise, I would say that the width of the confidence interval is -- is one of the -- one of the variables that affects the precision or the width of the confidence interval or the number of events or cases, which -- which could be related to sample size.

Q And you agree, Doctor, that high variability can also affect the confidence interval?

A That is also one of the other parameters that can affect the confidence interval, yes.

Q And, Doctor, when you're talking about sample size, let me just give you a hypothetical. If there were 5,000 patients in a -- in a cohort study and somebody is studying the number of pancreatic cancers, for example, let's say there's 14, do you -- is it your contention that the 14 is the sample size or the 5,000 cohort members?

A Again, to be more precise, in many cases, sample size is a function of the number of cases as well. So I mean, usually if you have a larger sample size for many conditions, let's say, heart attacks, the more people you follow up, the more people are going to have heart attacks.

So in this situation, sample size and

number of events are sort of directly proportional. But there are situations such as cancer where you have a large sample size, but you still have a small number of events. So what affects the precision of confidence interval is mostly -- it can be a sample size issue, but it's mostly directly related to the number of events or cases.

Q Doctor, you mentioned several times yesterday that the P value, according to the ASA, has -- has lost importance; is that a fair characterization?

A Well, it's still being used and accepted by many journals, but what I -- I believe I said was that the ASA has warned on the interpretation of what the P value is and what it is not.

Q Yes, sir. And the P value is simply the probability that results such as those actually observed in the study could arise under the null hypothesis? That's what a P value is, correct?

A Yes.

Q And what is the null hypothesis in the Hidajat study, Doctor?

MR. NIGH: Form objection.

THE WITNESS: The null hypothesis --

hypothesis would be that there is no risk of NDMA with cancer deaths.

BY MR. FOWLER:

Q Did you operate under a null hypothesis in your research and report drafting in this case, sir?

MR. NIGH: Form objection.

THE WITNESS: No, because null hypotheses are done when you actually want to do an -- a true experiment. When you're looking at observational studies you don't -- you don't have a -- I mean, you don't start with a null hypothesis. You -- you would form a hypothesis, but null hypotheses are mostly related to when you're designing your randomized trial and you want to calculate your sample size. And you have --

THE COURT REPORTER: I'm sorry, what? I'm sorry. Can you repeat the end of your answer?

THE WITNESS: What part of it did you want me to repeat?

THE COURT REPORTER: The hypotheses are mostly related to designing your randomized trial and you want to calculate your sample

size. And you have...

THE WITNESS: Yeah. So a null hypothesis is mainly used in a true -- in a randomized trial or a true experiment. When you want to calculate your power of the study, the null hypothesis is important. But for observational studies where I'm reviewing literature on a specific topic, I don't really see why a null hypothesis would be beneficial.

BY MR. FOWLER:

Q Doctor, when there are studies that are based on hospitalized patients, you agree that there is a bias to the -- the self-reporting from those patients? Do you understand the question?

MR. NIGH: Form objection.

THE WITNESS: I understand your question, but you have to be very specific, because self -- I mean, if it's a hospital-based study and both cases and controls are in the hospital, then you wouldn't have a self-reporting limitation.

So it -- it's -- you have to have the very specifics of the study, and then you have to show exactly where a limitation of bias would affect the outcome. I mean, I don't want

to make generalizations on a hospital-based study.

BY MR. FOWLER:

Q Sure. Let me try it this way: For a lung cancer patient who's being presented with a survey to complete which may help them understand the cause of their lung cancer, do you believe that that creates a reporting bias from the patient?

MR. NIGH: Form objection.

THE WITNESS: The reporting bias would only occur if the patient also believed that the -- and these questionnaires are very long. It's not about, you know, did you take this or that. They -- they covered a whole host of different items. So unless a patient knows that a specific item is linked to the -- to their lung cancer, then no, I won't -- I wouldn't see any sort of a differential bias in that situation in terms of the cases and many controls.

BY MR. FOWLER:

Q Okay.

MR. FOWLER: I'm going to mark Exhibit 30. It's an article applying the Bradford Hill criteria in the 21st century.

Steve, can you load that up?

(Whereupon, Exhibit 30 was marked for Identification.)

THE WITNESS: Do you mind if I take a break after your question with the article?

MR. FOWLER: Yes, this will be -- my last series of questions will be on this article and I'm done, sir. Can you make it 10 minutes?

THE WITNESS: Absolutely.

MR. FOWLER: Thank you.

MR. HARKINS: Introduced as Exhibit 30, if we can screen share.

THE WITNESS: Let me just -- I'm having trouble.

BY MR. FOWLER:

Q There it is. Can you see that now?

A Yes.

Q Okay. Thank you. Do you recognize -- have you seen this article before, Doctor?

A I may have. I'm not sure.

Q Do you agree or disagree that when doing an analysis using the Bradford Hill criteria, that it is appropriate to look to scientific articles in addition to epidemiologic articles when

assessing any of these criteria?

A What do you mean -- what do you mean between scientific article versus epidemiological articles?

Q Fair point, sir.

Do you agree that studies -- molecular studies, toxicology studies are appropriate to consider along with epidemiology studies when analyzing something under the Bradford Hill criteria?

MR. NIGH: Form objection.

THE WITNESS: I believe it depends on the question you're trying to ask. If your question is a general causation question and part of the Bradford Hill criteria requires a biologic plausibility, which usually requires a sort of mechanistic explanation, from animal studies. Then I don't think one would need -- for this specific question, need to go any further examining, you know, other than that mechanistic part of the Bradford Hill that requires some evidence of a mechanism from animal studies.

Beyond that, I don't think this question warrants further review of, you know,

complicated toxicological studies because, again, it -- the question doesn't really mean that. The question is on general causation. So I would -- I would maybe shorten my answer, if you will. It depends on the question.

For the question that I answered, I don't believe that those types of studies were necessary.

BY MR. FOWLER:

Q Thank you.

Let me direct your attention to criteria five, biologic gradient.

MR. FOWLER: I think it's on like the fifth or sixth page, please. There are no page numbers on mine.

BY MR. FOWLER:

Q Okay, sir. Do you see that Hill, referring to Sir Bradford Hill, wrote that, "If the dose response is seen, it is more likely that an association is causal."

Do you see that, sir?

A Yes.

Q And if you look about five lines down you see, "However, Hill acknowledged that the more complex dose-response relationships may exist, and

modern studies have confirmed that a monotonic dose response curve is an overly simplistic representation of most causal relationships."

Do you agree with that, sir?

MR. NIGH: Form objection. Agree that that's what it says or agree with that statement?

MR. FOWLER: Thank you.

BY MR. FOWLER:

Q Do you agree with that statement?

A Again, I think Hill is presenting a very general idea, and I -- it could be true for some instances and perhaps not for others.

Q Do you believe that -- strike that.

Let me just look a little bit further down.

You see after Footnote 9, "Integration of advanced statistical capabilities, data modeling techniques and knowledge from understanding of biomolecular interactions have resulted in the descriptions of more defined dose response curves capable of showing molecular effects at very low levels of exposure."

Do you agree that that -- that understanding the molecular effects at very low

levels of exposure for your analysis here would be important?

MR. NIGH: Form objection.

THE WITNESS: Again, these are not from Bradford Hill himself. I believe these are the opinions of the authors, correct?

BY MR. FOWLER:

Q I'm asking if you agree with that -- that statement, sir.

A Well, I want to -- I mean, I think it's important to sort of establish that these are -- what we have here on this screen and I'm reading, are the opinions of the authors of this paper.

MR. NIGH: Doctor, you have a right -- you have a right to look at this document. You can upload it, remember, and look at it. That's why it's put into chat.

THE WITNESS: Okay.

BY MR. FOWLER:

Q My question, Doctor, just so you keep it top of mind -- of course, you can look at whatever you like.

Do you agree that it would have been important for forming your opinions in this case to

understand the molecular effects at very low level of exposure to NDMA and NDEA?

MR. NIGH: Form objection.

THE WITNESS: No. I don't agree because, again, I was looking at a general causation question of exposure of NDMA over a long period. You know, it could have been three years, five years, up to 40 years. That was my question.

And what these authors are -- are, I believe, arguing, does not -- does not talk about any specific type of question, does not talk about the -- you know, the type of exposure, the -- the risk of cancer, the type of risk of cancer or the -- or the follow-up involved.

So for my specific question that I set out to answer, I don't believe any -- I mean, if there -- if there was any specific modeling data, I would have looked at it. But I don't believe that would negate looking at studies that looked at -- at those responses.

And by the way, the Hidajat studies did quite a sophisticated dose response analysis. So, again, I -- I don't quite

understand what these authors are -- are referring to when they're talking about modeling, because statistical dosing modeling was done in some of the studies that I included.

BY MR. FOWLER:

Q I want to show you the paragraph that starts, "Biological gradient." It's just down below this box.

Doctor, "Biological gradient is an example of how data integration can complicate causal inference." Do you agree with that description of the Bradford Hill criteria, biologic -- biological gradient?

A Yes.

Q And if you look three lines -- strike that.

The next sentence, "New tools and technical capabilities have allowed researchers to characterize a variety of low level molecular end points that may not lead to disease or observable outcomes on a larger scale."

Did I read that correctly, Doctor?

A Yes, I'm just rereading it.

Q Yes, sir.

And it says further down, "Thus molecular changes within the no observable adverse effect level may not contribute to disease and are more indicative of a threshold dose."

Doctor, with that backdrop, did you make any attempt to determine whether there is a no observable effects level for low doses of NDMA or NDEA?

MR. NIGH: Form objection.

THE WITNESS: Again, that wasn't the question that I set out to answer. The question that I set out to answer was -- was exposure to NDMA over a long period of time, high dose versus low dose, has a differential risk of cancer. What they're talking about here are -- again, they don't really specify the type of studies, the type of exposure. I think they're making very -- very general statements on the very large sort of scope of topics.

BY MR. FOWLER:

Q And do you believe, Doctor, that the biological gradient of the Bradford Hill criteria can be satisfied when evaluating NDMA and NDEA without an understanding of any threshold dose

level?

MR. NIGH: Form objection.

THE WITNESS: I think threshold dose levels are a very technical, specific question with respect to NDMA and cancer. The more general question that's sort of the umbrella question that I was set up to look at was, generally speaking, does exposure to NDMA over a long period cause cancer. And I don't believe that you need -- I mean, they were -- statistical modeling was used in the studies. But I don't -- I don't think you specifically need sophisticated tools or modelings to set out the question that I -- that I wanted to answer.

BY MR. FOWLER:

Q Well, Doctor, looking at the first part of this criteria five, it states that Sir Bradford Hill -- it says, "However, Hill acknowledged that more complex dose relationships may exist."

Did you consider that when trying to evaluate the biological gradient for NDMA, sir?

MR. NIGH: Form objection.

THE WITNESS: Again, I did not have,

you know, data on NDMA gradient or doses.
My -- my question was to look at the literature and answer the question whether long-term exposure to NDMA causes cancer. Again, I go back to what I mentioned a few minutes -- seconds ago.
BY MR. FOWLER:
Q Yes, sir.
A Your -- your question I believe is looking at a more specific type of a question.
For a general causation question, I do not believe that -- and, again, with Bradford Hill's statement here, which is very general, I do not believe that for the question that I set out to do, I needed that information that you mentioned.
Q Thank you.
MR. FOWLER: I have nothing further, sir. I think we have left some time remaining for any follow-up questions. Thank you for your time over these two days. I appreciate it.
THE WITNESS: Thank you.
MR. NIGH: Do we have anybody else that's asking questions on the defense side? Steven, do you know?

MR. FOWLER: No, sir. I don't believe we do.

MR. NIGH: Okay. Can we get a -- are we on the record, or can we go off the record?

THE VIDEOGRAPHER: Yes. The time is now 11:09. We're going off the record.

(Whereupon, a short break was taken.)

THE VIDEOGRAPHER: The time is now 11:27. We're back on the record.

MR. NIGH: Steven, this is -- in response to your question earlier about not being on camera, I didn't want to be short with you, and I did want to give you a reason. My daughter has been -- was diagnosed with COVID about a week and a half ago. I think that's the timing. And so, frankly, I have had to do -- and defend the deposition remotely. So I don't have the same sort of bandwidth that I have in my office. And with that, we have had some storms that have rolled through both yesterday and today. And when I'm on -- not on video, but just speaking, then it doesn't have as much breakup.

So I think right now, it's probably okay. The weather is a little bit better

outside, but I figured I'd give you that explanation since you asked. And I know that we have had, you know, multiple other past depositions where the one making objections has not appeared on camera.

MR. FOWLER: Thank you. And best wishes for you daughter's recovery. I'm sorry to hear that.

MR. NIGH: Yes, thank you.

At this time, we do -- we're not going to ask any questions, and so I'd like to thank Dr. Etminan for his time. And I think that this time, you're free to go. Thank you.

THE VIDEOGRAPHER: The time is now 11:27. This ends today's deposition. Thank you. Thank you all.

THE COURT REPORTER: Counsel, does anybody want copies?

MR. NIGH: We will want one copy. It can come to me on the plaintiff's side, I don't know if you have my information already -- and then we do want a -- we do want to read the transcript --

THE COURT REPORTER: Sure.

Any other counsel?

MR. GALLAGHER: Duane Morris would like a copy. I think we're already set up to get one, but just in case.

MR. HARKINS: Same for Greenberg Traurig. If you don't have an order for us, we certainly want a copy.

MS. KAPKE: Jamie, this is Kara from CVS and Rite Aid. I'll take a copy, just regular delivery, etrans.

MR. TRISCHLER: This is Clem Trischler from Mylan. I think we have -- we should have a standing order for all depositions, so we would want that. But if we don't, or if you don't have that, we do want a copy.

THE COURT REPORTER: Counsel, anyone else?

MR. SHAH: This is Nakul Shah for Hetero Drugs and Hetero Labs. We would like a final version of the transcript as well.

THE COURT REPORTER: Okay. Anything else, counsel?

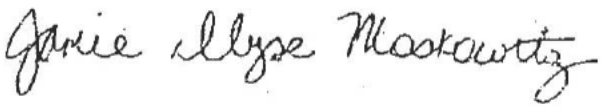
(Whereupon, the deposition concluded at 11:27 a.m.)

C E R T I F I C A T E

I, Jamie I. Moskowitz, a Shorthand (Stenotype) Reporter and Notary Public, do hereby certify that the foregoing Deposition, of the witness, MAHYAR ETMINAN, taken at the time and place aforesaid, is a true and correct transcription of my shorthand notes.

I further certify that I am neither counsel for nor related to any party to said action, nor in any way interested in the result or outcome thereof.

IN WITNESS WHEREOF, I have hereunto set my hand this 2nd day of September, 2021.



Jamie Ilyse Moskowitz

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Daniel A. Nigh, Esq.
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September 2, 2021.

RE: In Re: Valsartan, Losartan, Et Al v.
8/25/2021, Mahyar Etminan (#4772413)

The above-referenced transcript is available for review.

Within the applicable timeframe, the witness should read the testimony to verify its accuracy. If there are any changes, the witness should note those with the reason, on the attached Errata Sheet.

The witness should sign the Acknowledgment of Deponent and Errata and return to the deposing attorney. Copies should be sent to all counsel, and to Veritext at cs-ny@veritext.com.

Return completed errata within 30 days from receipt of testimony.

If the witness fails to do so within the time allotted, the transcript may be used as if signed.

Yours,
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In Re: Valsartan, Losartan, Et Al v.

Mahyar Etminan (#4772413)

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Mahyar Etminan Date

In Re: Valsartan, Losartan, Et Al v.
Mahyar Etminan (#4772413)

ACKNOWLEDGEMENT OF DEPONENT

I, Mahyar Etminan, do hereby declare that I have read the foregoing transcript, I have made any corrections, additions, or changes I deemed necessary as noted above to be appended hereto, and that the same is a true, correct and complete transcript of the testimony given by me.

_____ _____

Mahyar Etminan Date

*If notary is required

SUBSCRIBED AND SWORN TO BEFORE ME THIS

_____ DAY OF _____, 20___.

_____

NOTARY PUBLIC